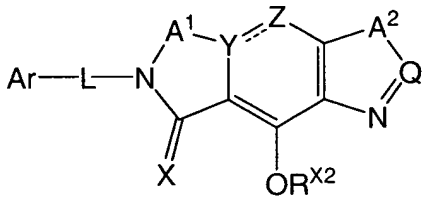
Amendment to the Specification

SUMMARY OF THE INVENTION

The present invention provides compositions and methods for inhibition of HIV integrase.

In one aspect, the invention ~~comprises~~ is a compound having the structure:

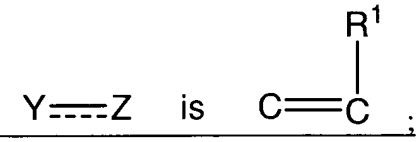


wherein:

A^1 is independently selected from $C(R^2)_2$, CR^2OR, $CR^2OC(=O)R$, $C(=O)$, $C(=S)$, CR^2SR, and $C(=NR)$,

A^2 is independently selected from $C(R^2)_2$–$C(R^3)_2$, $C(R^2)=C(R^3)$, and $C(=O)C(R^3)_2$;

Q is CR^4;

Y---Z is 

;

L is selected from a bond, O, S, S–S, S(=O), $S(=O)_2$, $S(=O)_2NR$, NR, N–OR, C_1–C_{12} alkylene, C_1–C_{12} substituted alkylene, C_2–C_{12} alkenylene, C_2–C_{12} substituted alkenylene, C_2–C_{12} alkynylene, C_2–C_{12} substituted alkynylene, C(=O)NH, OC(=O)NH, NHC(=O)NH, C(=O), $C(=O)NH(CH_2)_n$, or $(CH_2CH_2O)_n$, where n is optionally 1, 2, 3, 4, 5, or 6;

X is selected from O, S, NH, NR, N–OR, $N–NR_2$, $N–CR_2OR$ and $N–CR_2NR_2$;

Ar is selected from (a) a C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl;

or (b) a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms;

R^2, R^3 and R^4 are each independently selected from H, F, Cl, Br, I, OH, $–NH_2$, $–NH_3^+$, –NHR, $–NR_2$, $–NR_3^+$, C_1–C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1–C_8 alkylsulfonate, C_1–C_8 alkylamino, 4-dialkylaminopyridinium, C_1–C_8

alkylhydroxyl, C_1–C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, $-SOAr$, $-SAr$, $-SO_2NR_2$, $-SOR$, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, $-CN$, $-N_3$, $-NO_2$, C_1–C_8 alkoxy, C_1–C_8 trifluoroalkyl, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

when taken together on a single carbon, two R^2 or two R^3 may form a spiro ring; R^1 is independently selected from CR_3, $NRSO_2R$, $OC(=O)NR_2$ $OC(=O)R$, SR, H, F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, $-NHR$, $-NR_2$, $-NR_3^+$, C_1–C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1–C_8 alkylsulfonate, C_1–C_8 alkylamino, 4-dialkylaminopyridinium, C_1–C_8 alkylhydroxyl, C_1–C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, $-SOAr$, $-SAr$, $-SO_2NR_2$, $-SOR$, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, $-CN$, $-N_3$, $-NO_2$, C_1–C_8 alkoxy, C_1–C_8 trifluoroalkyl, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

R is independently selected from H, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

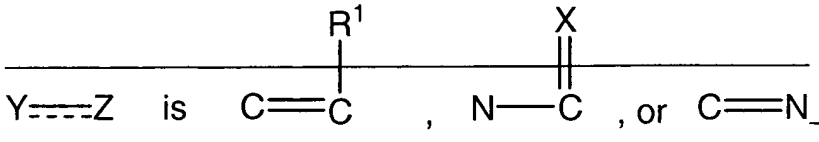
R^{X2} is independently selected from H, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, a prodrug moiety, and a protecting group;

and the tautomers, salts, solvates, resolved enantiomers and purified diastereomers thereof;

with the proviso that when Y=Z is C=C(OH), X is O, A^1 is C(=O), A^2 is $C(R^2)=C(R^3)$, and Q is CH, then L is not a bond.

A^1 and A^2 are independently selected from O, S, NR, $C(R^2)_2$, CR^2OR, $CR^2OC(=O)R$, C(=O), C(=S), CR^2SR, C(=NR), $C(R^2)_2$–$C(R^3)_2$, $C(R^2)=C(R^3)$, $C(R^2)_2$–O, NR–$C(R^3)_2$, $N=C(R^3)$, N=N, SO_2–NR, $C(=O)C(R^3)_2$, C(=O)NR, $C(R^2)_2$–$C(R^3)_2$–$C(R^3)_2$, $C(R^2)=C(R^3)$–$C(R^3)_2$, $C(R^2)C(=O)NR$, $C(R^2)C(=S)NR$, $C(R^2)=N$–$C(R^3)_2$, $C(R^2)=N$–NR, and $N=C(R^3)$–NR;

~~Q is N, $^+$NR, or CR^4;~~



Y----Z is C=C , N—C , or C=N;

L is selected from a bond, O, S, S–S, S(=O), $S(=O)_2$, $S(=O)_2NR$, NR, N–OR, C_1–C_{12} alkylene, C_1–C_{12} substituted alkylene, C_2–C_{12} alkenylene, C_2–C_{12} substituted alkenylene, C_2–C_{12} alkynylene, C_2–C_{12} substituted alkynylene, C(=O)NH, OC(=O)NH, NHC(=O)NH, C(=O), $C(=O)NH(CH_2)_n$, or $(CH_2CH_2O)_n$, where n may be 1, 2, 3, 4, 5, or 6;

X is selected from O, S, NH, NR, N–OR, N–NR_2, N–CR_2OR and N–CR_2NR_2;

Ar is selected from C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl;

R^1, R^2, R^3 and R^4 are each independently selected from H, F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, –NHR, $-NR_2$, $-NR_3^+$, C_1–C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1–C_8 alkylsulfonate, C_1–C_8 alkylamino, 4-dialkylaminopyridinium, C_1–C_8 alkylhydroxyl, C_1–C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, –SOAr, –SAr, $-SO_2NR_2$, –SOR, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, –CN, $-N_3$, $-NO_2$, C_1–C_8 alkoxy, C_1–C_8 trifluoroalkyl, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

when taken together on a single carbon, two R^2 or two R^3 may form a spiro ring; and

R is independently selected from H, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

R^{X2} is independently selected from H, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, a prodrug, a pharmaceutically acceptable prodrug, a prodrug moiety, a protecting group, and a phosphonate prodrug moiety;

and the salts, solvates, resolved enantiomers and purified diastereomers thereof;

with the proviso that when Y=Z is C=C(OH), X is O, A^1 is C(=O), A^2 is $C(R^2)=C(R^3)$, and Q is CH, then L is not a bond.